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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/003,468	10/23/2001	Fatemeh Mojtabai	FMI-001RCE	4328

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EXAMINER

SMITH, CAROLYN L

ART UNIT	PAPER NUMBER
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1631

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/003,468	Applicant(s) MOJTABAI, FATEMEH	
	Examiner Carolyn Smith	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 July 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-6,8,63,64,67-71 and 74-76 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-6,8,63,64,67-71 and 74-76 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's amendments and remarks, filed 7/21/08, are acknowledged. Amended claims 1, 8, 63, 64, cancelled claims 2, 7, 9-62, 65-66, and 72-73 and new claims 74-76 are acknowledged. In the remarks section, Applicant states that claim 66 will be pending; however, it is noted that this claim was cancelled (see listing of claims).

Applicant's arguments, filed 7/21/08, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from the previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1, 3-6, 8, 63-64, 67-71, and 74-76 are herein under examination.

Claim Rejections - 35 USC § 112, Second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 69-71, and 74 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These rejections are necessitated by amendment.

Claim 3 recites the limitation "amphiphilic molecule" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim as there is no previous mention of "amphiphilic molecule". Clarification of this issue via clearer claim wording is requested. Claims 69-71 are also rejected due to their dependency from claim 3. This rejection is necessitated by amendment.

Claim 74 recites the limitation "said protein's" in line 1. There is insufficient antecedent basis for this limitation in the claim. While there is previous mention of plural "proteins", there is no previous mention of a single "protein". Therefore, it is unclear to which particular protein is being referred to in "said protein's". Clarification of this issue via clearer claim wording is requested.

Claim 74 (lines 5-6) recite "that a two-dimensional ordered array of said proteins is formed" and then mention using "said two- or three- dimensional ordered array" which is confusing. If only a two-dimensional ordered array is formed, it is unclear what Applicant means by using a "three-dimensional ordered array". Clarification of this issue via clearer claim wording is requested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, 5, 8, 67, and 74-75 are rejected under 35 U.S.C. 102(b) as being anticipated by RIBI (US 4859538). This rejection is maintained for claims 1, 4, 5, 8, and 67 and necessitated by amendment for claims 74-75.

RIBI teaches a method of constructing 2 and 3 dimensional ordered (crystalline) arrays of proteins by contacting an air-water interface with a lipid composition comprising a protein, and

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allowing the mixture to incubate under spreading (i.e. lateral) pressure until the crystals (array) form wherein the aqueous protein solution has a salt concentration (i.e. not a detergent) (see examples at col. 9, line 62-col. 10, line 39, col. 11, line 55-col. 12, line 8, and col. 12, line 50-col. 13, line 22; claim 9; col. 4, third paragraph). RIBI specifically teaches that with regard to a B1 reductase protein, "Crystals were formed at the air-water interface" at column 10, line 25, thus claims 1, 4, 5, 8, and 67 are anticipated. RIBI specifically teaches application of lateral pressure (col. 7, lines 31-37) and teaches that surfactants (i.e. not necessarily detergents) and polymers are not necessary to get ordered protein arrays (column 4, third paragraph; column 7, lines 43-45), therefore the pressure applied is inherently above whatever critical density point is required for formation of a 2D or 3D ordered array. RIBI discloses structure resolution of 5 Å or higher (col. 3, third and fourth paragraphs; col. 12, second and third paragraphs), as stated in instant claim 74. RIBI discloses surfactant lacking ligand to form an array with proteins (col. 7, third paragraph; col. 3, last paragraph), as stated in instant claim 75.

Thus, RIBI anticipates claims 1, 4, 5, 8, 67, and 74-75.

Applicant summarizes the invention. Applicant summarizes RIBI. Applicant argues that RIBI states throughout the application that his invention "requires a specific binding between the ligand bound to the surfactant and the protein". It is noted that instant claim 1 does not preclude the use of a ligand. It is also noted that RIBI discloses surfactant lacking ligand to form an array with proteins (col. 7, third paragraph; col. 3, last paragraph). Applicant argues that RIBI's application is directed to soluble proteins which are further solubilized using surfactants and other detergents. It is noted that instant claim 1 does not preclude soluble proteins. It is further

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noted that RIBI provides a list of a variety of surfactants that may be used by themselves or in combinations (col. 4, third paragraph) which includes entities that are not considered to be detergents by one skilled in the art. Applicant argues that RIBI fails to teach a method for forming a two- or three-dimensional ordered array of water insoluble proteins. This statement is considered moot as this limitation is not found in the currently rejected claims in the 35 USC 102 rejection above. It will be addressed in the 35 USC 103 rejection below.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 4, 5, 6, 8, 67, and 74-75 are rejected under 35 U.S.C. 103(a) as being unpatentable over RIBI (US 4859538) in view of OHLSSON et al. (Bioelectrochemistry and Bioenergetics (1995) vol. 38, pp. 137-148). This rejection is maintained for claims 1, 4, 5, 6, 8, 67 and necessitated by amendment for claims 74-75.

RIBI teaches a method of constructing 2 and 3 dimensional ordered (crystalline) arrays of proteins by contacting an air-water interface with a lipid composition comprising a protein, and

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allowing the mixture to incubate under spreading (i.e. lateral) pressure until the crystals (array) form wherein the aqueous protein solution has a salt concentration (i.e. not a detergent) (see examples at col. 9, line 62-col. 10, line 39, col. 11, line 55-col. 12, line 8, and col. 12, line 50-col. 13, line 22; claim 9; col. 4, third paragraph). RIBI specifically teaches that with regard to a B1 reductase protein, “Crystals were formed at the air-water interface” at column 10, line 25, as stated in claims 1, 4, 5, 8, and 67. RIBI specifically teaches application of lateral pressure (col. 7, lines 31-37) and teaches that surfactants (i.e. not necessarily detergents) and polymers are not necessary to get ordered protein arrays (column 4, third paragraph; column 7, lines 43-45), therefore the pressure applied is inherently above whatever critical density point is required for formation of a 2D or 3D ordered array. RIBI disclose structure resolution of 5 Å or higher (col. 3, third and fourth paragraphs; col. 12, second and third paragraphs), as stated in instant claim 74. RIBI discloses surfactant lacking ligand to form an array with proteins (col. 7, third paragraph; col. 3, last paragraph), as stated in instant claim 75. RIBI specifically teaches crystallization of subunit B1 of a ribonucleoside reductase at an “air-water interface” in the presence of lipids, wherein surface pressure is applied to the air-water interface (col. 10, lines 7-31). RIBI further teaches that a variety of proteins, including membrane proteins may be crystallized in his method (col. 4, lines 51-62 and col. 8, lines 42-50). RIBI does not specifically teach use of proteoliposomes in his method.

OHLSSON teaches that cholera toxin may be bound to proteoliposomes on a surface, and will retain its activity when so bound (abstract), as stated in instant claim 6.

It would have been obvious to one of ordinary skill in the art at the time of invention to have crystallized the membrane proteins of RIBI using the proteoliposomes of OHLSSON in the

lipid layer in the method of RIBI where the motivation would have been to crystallize the proteins in the method of RIBI in an active conformation, as suggested by the teaching of OHLSSON that proteoliposomes aid in retaining biological activity of at least one membrane protein (abstract).

Thus, RIBI in view of OHLSSON make obvious instant claims 1, 4, 5, 6, 8, 67, and 74-75.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 3, 63-64, 68-71, and 76 are rejected under 35 U.S.C. 103(a) as being unpatentable over RIBI (US 4859538) in view of OHLSSON et al. (Bioelectrochemistry and Bioenergetics (1995) vol. 38, pp. 137-148) as applied to claims 1, 4, 5, 6, 8, 67, and 74-75 above, and further in view of Bamdad et al. (US 2005/0112607). This rejection is necessitated by amendment.

RIBI teaches a method of constructing 2 and 3 dimensional ordered (crystalline) arrays of proteins by contacting an air-water interface with a lipid composition comprising a protein, and allowing the mixture to incubate under spreading (i.e. lateral) pressure until the crystals (array) form wherein the aqueous protein solution has a salt concentration (i.e. not a detergent) (see examples at col. 9, line 62-col. 10, line 39, col. 11, line 55-col. 12, line 8, and col. 12, line 50-

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col. 13, line 22; claim 9; col. 4, third paragraph). RIBI specifically teaches that with regard to a B1 reductase protein, "Crystals were formed at the air-water interface" at column 10, line 25, in the presence of lipids (col. 10, lines 7-31), as stated in instant claims 1, 4, 5, 8, and 67. RIBI specifically teaches application of lateral pressure (col. 7, lines 31-37) and teaches that surfactants (i.e. not necessarily detergents) and polymers are not necessary to get ordered protein arrays (column 4, third paragraph; column 7, lines 43-45), therefore the pressure applied is inherently above whatever critical density point is required for formation of a 2D or 3D ordered array, as stated in instant claims 3, 64, 68, and 70. RIBI further teaches that a variety of proteins, including membrane proteins may be crystallized in his method (col. 4, lines 51-62 and col. 8, lines 42-50). RIBI describe structure resolution of 5 Å or higher (col. 3, third and fourth paragraphs; col. 12, second and third paragraphs), as stated in instant claim 74. RIBI describes surfactant lacking ligand to form an array with proteins (col. 7, third paragraph; col. 3, last paragraph), as stated in instant claim 75. RIBI does not specifically teach use of proteoliposomes in his method or water insoluble membrane proteins.

OHLSSON teaches that cholera toxin may be bound to proteoliposomes on a surface, and will retain its activity when so bound (abstract), as stated in instant claims 6, 63, and 71.

OHLSSON does not specifically describe water insoluble membrane proteins.

BAMDAD teaches a relatively ordered assembly of molecules to form an ordered array (0092), using water insoluble membrane proteins (0004, 0005, 0161, 0230), and not requiring detergent (0034).

It would have been obvious to one of ordinary skill in the art at the time of invention to have crystallized the membrane proteins of RIBI using the proteoliposomes of OHLSSON in the

lipid layer in the method of RIBI where the motivation would have been to crystallize the proteins in the method of RIBI in an active conformation, as suggested by the teaching of OHLSSON that proteoliposomes aid in retaining biological activity of at least one membrane protein (abstract). It would have been further obvious to one of ordinary skill in the art at the time the invention was made to not use water insoluble membrane proteins that do not require detergents as stated by BAMDAD wherein the motivation would have been to avoid interference with binding reactions and allow for rapid and sensitive detection and analysis of biomolecular interactions to facilitate drug discovery, as stated by BAMDAD (0002, 0034).

Thus, RIBI in view of OHLSSON and BAMDAD make obvious instant claims 1, 3-6, 8, 63-64, 67-71, and 74-76.

Applicant summarizes instant claims 1, 4, 6, 63, 69, and 71. Applicant argues that RIBI and OHLSSON do not teach water insoluble membrane proteins. This argument is deemed moot due to the presence of BAMDAD which recites this limitation.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

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MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. If you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, please call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran, can be reached on (571) 272-0720.

October 22, 2008

/Carolyn Smith/
Primary Examiner
AU 1631